Peri-operative management of patients with diabetes

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This is an important but often neglected topic that is frequently poorly managed. Too often peri-operative care is left in the hands of nursing staff in the ward, following the anaesthetist's peri- and postoperative instructions. These instructions usually take the form of a crude generic sliding scale adapted to fit comfortably into the usual six-hourly patient monitoring that occurs in most wards. This form of care is wrong in every possible way and should be actively discouraged by everyone involved in patient care, from the nursing staff to the surgeon and anaesthetist, and even the attending physician, if involved.

'Why bother with good glycaemic control; surely a few days of erratic or high sugar levels cannot do any real harm?' This seems to be the pervasive attitude that has crept into much of routine medical care in the peri-operative period. A similar attitude prevailed, until a few years ago, with regard to the care needed to prevent venous thrombo-embolism in the peri-operative period. Through education and new guidelines, our attitudes and practices to prevent venous thrombo-embolism have changed dramatically. A similar change is now needed with regard to what is considered to be routine practice in the care of diabetes in the peri-operative period.

There is a large body of observational evidence linking in-hospital hyperglycaemia to poorer outcomes. There is also a growing body of evidence in the form of cohort studies and even some early randomised, controlled trials showing that intensive treatment of hyperglycaemia in hospital improves outcomes.[1,2,3]

The most famous study analysing tight glycaemic control in the peri-operative period was a single-centre study which reported a 42% reduction in ICU mortality.[2] Recent multi-centre studies in both medical and surgical patients have failed to demonstrate the same benefits; in fact the outcomes in the intensive groups were slightly worse.[4] However closer examination of the largest of these trials reveals that the difference between intensive and standard care was very small; blood sugar levels of 6.4 versus 8%. These trials do not suggest that intensive target glucose control is not important or causes harm but rather that the target chosen for tight control may have been a little too ambitiously low, with the resultant frequent hypoglycaemia contributing to the increase in adverse outcomes.

A recent meta-analysis of 26 trials[5] assessed care of hospitalised diabetic patients, with intensive glucose control (glucose target 4.5–6 mmol/l) versus conventional control (glucose target 7.8–10 mmol/l). The relative risk (RR) of death was 0.93, favouring conventional control. About 50% of the trial participants reported hypoglycaemia, with a pooled RR of 6 for hypoglycaemia in the intensive-control group.

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This suggests that the reason for the negative outcome of the trials of intensive treatment in hospitalised diabetics may be due to the inevitable increase in hypoglycaemia. This trend has also been seen in outpatient-care trials of intensive versus standard care in diabetics. The ADVANCE, ACCORD and VADT trials of intensive versus standard care in diabetics with a high risk of cardiovascular disease all showed an increase in mortality in the intensive-control groups. Subsequent meta-analyses have shown that in these groups, this incidence of hypoglycaemia was significantly higher than in the standard-care groups, suggesting this was the possible cause for the negative outcomes.

It may be reasonable therefore to say that hypoglycaemia should be avoided in these patients at the expense of tight glycaemic control. It seems that high-risk patients in both in- and out-patient settings are more vulnerable to the severe adverse outcomes of hypoglycaemia.

Interestingly, both the meta-analysis mentioned above,[5] and randomised, controlled trials[2,6,7] show that critically ill surgical patients may actually benefit from tighter glycaemic control, whereas critically ill medical patients do not. This may be a reflection of the pre-hospital health of surgical and medical patients where, by their very nature, surgical patients are likely to have had better pre-admission health status and therefore be better able to tolerate the inevitable hypoglycaemia associated with tight glycaemic control.

How do we incorporate this information into guidelines for peri-operative care of diabetics?

See Tables 1 and 2 for definitions of hyper- and hypoglycaemia.

Where hyperglycaemia is discovered incidentally on routine testing of patients who have not previously been diagnosed with dysglycaemia or diabetes, these patients should be monitored and managed as if they were diabetic for the duration of the admission. Upon discharge, a formal plan for follow up of the impaired glucose metabolism should be made to assess if this was just a transient problem or one which will need further treatment and follow up.

Table 1. Hyperglycaemia.

	Hyperglycaemia	Diagnostic of diabetes
Fasting glucose level	> 5.9 mmol/l	> 7 mmol/l
Random glucose level	> 7.8 mmol/l	> 11.1 mmol/l
HbA_{1c} level	> 6%	> 6.5%

Note: these are laboratory values. Finger-prick values should prompt a formal laboratory test.

Table 2. Hypoglycaemia.

	Blood glucose (mmol/l)
Hypoglycaemia	< 3.9
Mild to moderate hypoglycaemia	2.2–3.9
Severe hypoglycaemia	< 2.2

Note: these are laboratory values. Finger-prick values should guide treatment but if there is doubt, confirm with a formal laboratory test.

As hypoglycaemia has been linked to increased mortality in hospitalised patients, especially high-risk patients, mild to moderate hypoglycaemia should be identified and treated promptly to avoid progression to a more severe episode, with possible severe consequences.

General treatment principles

Diabetic patients admitted to hospital should be clearly identified as such and this identification should trigger a pre-specified set of standardised protocols. The identification of patients as diabetics should be clear to all members of the care group, from food, kitchen and dietetics staff to the ward and theatre nursing staff, and even to the surgeons and anaesthetists involved in the surgical procedure itself.

Protocols should be available to all staff and should be as clear and simple as possible. They should also be able to cater for all types of diabetics from the brittle type 1 patient to the type 2 patient normally controlled on diet alone.

Critically ill patients

Evidence, expert opinion and guidelines by most national and international endocrine and diabetes associations recommend the use of insulin infusions in these patients, particularly in the intensive care unit (ICU) setting. Glucose targets should be 7.8–10 mmol/l in most patients, however less vulnerable and surgical patients may benefit from a slightly lower range of 6.1–10 mmol. The use of an intravenous infusion requires frequent glucose monitoring, not less than every two hours and preferably hourly, with adjustments made to the infusion rate depending on the glucose levels and trends.

Table 3. An appropriate peri-operative insulin regime.[9]

Basal–bolus insulin regimen

- Discontinue oral anti-diabetic drugs on admission
- Calculate the starting total daily dose (TDD):
  - 0.4 U/kg/d for admission blood glucose between 7.8 and 11.1 mmol/l
  - 0.5 U/kg/d × blood glucose between 11.2 and 22.2 mmol/l
- Half of TDD as insulin glargine (Lantus®) and half as rapid-acting analogue
- Insulin glargine once daily, at the same time of day
- Rapid-acting insulin analogue three equally divided doses with meals
- Supplemental insulin:
  - Give supplemental insulin (rapid-acting analogue) following the 'sliding-scale' protocol below for blood glucose 7.8 mmol/l.
  - If a patient is able and expected to eat all, give supplemental insulin (rapid-acting analogue) before each meal and at bedtime following the 'usual' column.
  - If a patient is not able to eat, give supplemental insulin (rapid-acting analogue) every six hours (6–12–6–12) following the 'insulin sensitive' column.

Blood glucose (mmol/l)	Insulin sensitive (units)	Usual (units)	Insulin resistant (units)
> 7.8–10	2	4	6
10.1–12.2	4	6	8
12.3–14.4	6	8	10
14.5–16.7	8	10	12
16.8–19.4	10	12	14
19.5–22.2	12	14	16
> 22.2	14	16	18

- Insulin adjustment:
  - If the fasting or mean blood glucose during the day is 7.8 mmol/l in the absence of hypoglycaemia, increase insulin glargine dose by 20% every day.
  - If a patient develops hypoglycaemia (3.9 mmol/l), decrease glargine daily dose by 20%.
- Blood glucose monitoring:
  - Measure blood glucose level before each meal and at bedtime (or every six hours if a patient is nil per os.

Non-critically ill patients

As randomised, controlled trials are lacking, guidelines in this group are based on clinical experience and judgement. Glucose targets in most patients controlled with insulin would be 7.8–10 mmol/l, providing these can be achieved with a low risk of hypoglycaemia. When glucose values frequently fall below 5.6 mmol/l, consideration should be given to modifying the treatment to avoid hypoglycaemia. When glucose values fall below 3.9 mmol/l, treatment must be modified to avoid more serious hypoglycaemic episodes.

In patients using insulin who have been stable prior to admission, in a tighter glycaemic range, lower limits may be acceptable in hospital and peri-operatively. Conversely, patients who are critically ill or in patient-care settings where frequent monitoring is not possible or feasible, less tight control may be acceptable.

Clinical judgement must be used when considering an acceptable range for patients where medications, nutritional status and severity of illness may influence what may be considered an acceptable glycaemic range.

Hypoglycaemic agents in peri-operative care

Insulin

This is the treatment of choice in hospitalised patients and in the peri-operative management of diabetics (Table 3).[8] Insulin should be given via insulin infusions in critically ill patients and in ICU care. Non-critically ill patients should be managed with subcutaneous insulin.

The method through which subcutaneous insulin is delivered is very important. A sliding-scale insulin regime (SSI) to control hyperglycaemia in hospitalised and peri-operative patients should never be used for more than a few hours. Prolonged use of sliding-scale insulin should be avoided for the following reasons:

- It is ineffective in the majority of patients.
- It increases the risk of both hyperglycaemia and hypoglycaemia.
- A recent randomised trial in general surgical patients with type 2 diabetes has shown that its use is associated with adverse outcomes.[9]
- It is potentially extremely dangerous in type 1 diabetes patients.[8]

A safe and effective subcutaneous insulin regime should deliver basal insulin that should be given, even in the fasting patient, to maintain normal glucose metabolism and avoid ketogenesis. Timed prandial doses should be given with meals. Allowance should be made for corrective doses to be given both with meals and at other times, should there be a need for this. A number of recently published protocols guiding insulin use in a variety of circumstances can be adapted for particular circumstances and patients.

Other hypoglycaemic agents

There are no safety data on the use of these agents in hospitalised and peri-operative care of patients. For this reason, as a general rule, these agents should be avoided and discontinued in the peri-operative period. Exceptions may be considered for patients who

are not particularly ill and are likely to be eating normally. These agents can be restarted prior to discharge once it is clear that the patient is recovering and will be ready for discharge soon.

- Metformin: this should be discontinued in anticipation of contra-indications to its use, which may be likely to arise in the peri-operative period. These include renal failure, unstable haemodynamics and the need for an imaging study, which will require contrast.
- Sulphonylureas: there are no safety data and the risk of prolonged hypoglycaemia in unstable patients who may not be eating is significant. It should be discontinued and only re-initiated once it is clear that the patient is stable, eating normally and is nearly ready for discharge.
- Thiazolidinediones are no longer considered to be safe hypoglycaemic agents, even in the outpatient setting and should be discontinued in the peri-operative period. Upon discharge, an alternative agent should be considered.
- DDP4 inhibitors: there are no safety data and they should be discontinued. Particular care should be taken with vildagliptin with renal impairment. It should only be restarted once the patient is stable, eating normally, is almost ready for discharge and renal function has been determined to be normal.
- GLP1 analogues: there are no safety data and these should be discontinued until the patient is stable, eating normally and nearing discharge.

Healthcare specialist's roles in the peri-operative period

Diabetes management may be under the care of the patient's general practitioner, a physician, an endocrinologist, the surgeon or the anaesthetist, depending on the circumstances and levels of experience. However, the use of appropriately trained specialists such as endocrinologists has been shown to reduce the length of stay, improve glycaemic control and improve outcomes.[3] Where available, their involvement should be sought for management of all diabetics in the hospital setting and especially the peri-operative period.

The patient's role in the peri-operative period

Patients who are fully conscious, well educated in diabetes care and have stable pre-operative glucose profiles should be encouraged to participate in the management of their diabetes in this period. Involvement may range from self monitoring of blood glucose and carbohydrate consumption to assuming full responsibility for their insulin treatment under the guidance of the healthcare team.

Planning discharge

This is not as simple as just sending the patient home and telling him/her to restart the usual medication. There are some very important points which need to be considered and guidelines to be adhered to:

- Care must be taken to be sure that the diabetic has stable glycaemic control on treatment that can be continued safely at home.
- If the patient is newly diagnosed or there has been significant change to the pre-admission treatment, care must be taken to ensure the patient understands the changes. This may not be appropriate for the surgeon to do and an endocrinologist consultation may be required.
- If required, consider:
  - dietician consultation to educate and plan the post-operative diet if significant changes are required.
  - diabetic educator if newly diagnosed or significant changes to medication or complications of diabetes have been detected.
- A discharge summary should be sent to the healthcare professional usually responsible for the patient's diabetes care.
- A follow-up appointment should be made with the healthcare professional responsible for the diabetes care, to ensure glycaemic control remains stable and to ensure compliance and adherence to treatment, especially if significant changes have been made.

Conclusion

There are a number of important factors to be considered and guidelines that need to be in place to ensure optimal care of patients in the peri-operative period. This will result in optimal outcomes. Most important is identification of the patient as a diabetic, and then planning treatment of the diabetes in the peri-operative period.

Other than in exceptional circumstances, most anti-diabetic agents, except insulin, should be discontinued. For patients not on insulin already, an appropriate regime should be planned. The use of sliding-scale insulin regimes should never be used for longer than a few hours and ideally all patients should be started on an appropriate basal–bolus regime with allowance made for corrective doses if needed.

Glycaemic control should not be too tight in the majority of patients, with a range of 6.1–10 mmol/l considered most appropriate for most patients. Hypoglycaemia should be avoided as it appears that this is linked to increased mortality. Appropriately trained specialists such as endocrinologists should be involved whenever possible. Appropriate education and understanding should be ensured and careful follow up and monitoring arranged prior to discharge.

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